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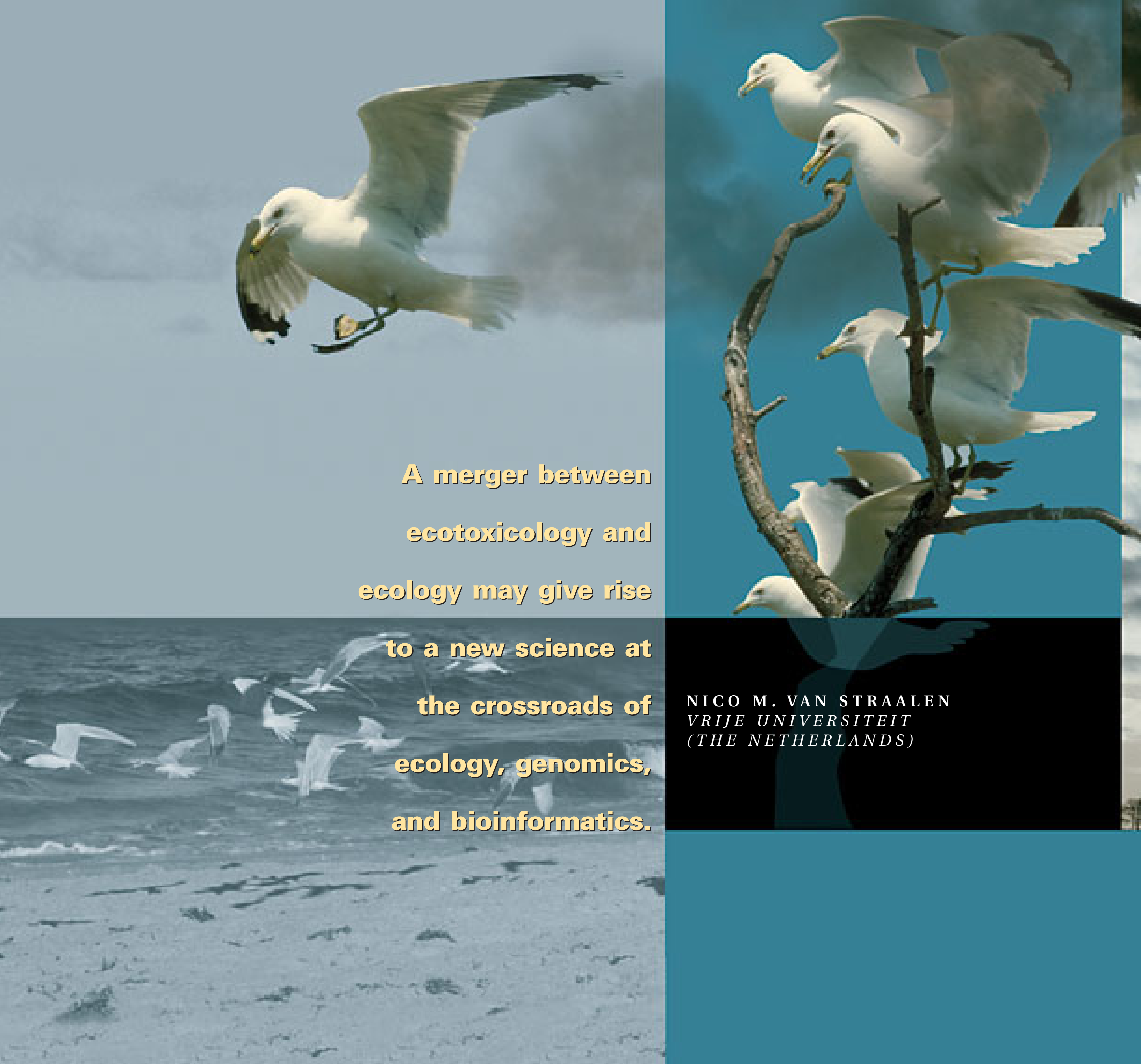
Ecotoxicology *Becomes* STRESS Ecology



A merger between ecotoxicology and ecology may give rise to a new science at the crossroads of ecology, genomics, and bioinformatics.

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Ecotoxicology was first developed in the 1970s by toxicologists with an interest in the environment (*1*). Consequently, the basic principles of the science were those of toxicology: experimental testing, analysis of dose–effect relationships, and estimation of effect concentrations, such as the exposure concentration at which 50% effect is observed within a certain period (EC_{50}). The "testing-based" approach of ecotoxicology greatly benefited environmental regulation by offering a solid basis for deriving maximum acceptable chemical concentrations. Handbooks document the various tests that have been developed (*2–4*), but the role of ecotoxicology extends beyond simple data collection.

Because the major environmental pollutants, at least in Europe and North America, are coming under the control of regulatory authorities and are declining, this part of ecotoxicology is now more or less completed. There is still work to do, because monitoring polluted sites, evaluating new chemical substances, and developing abatement scenarios will require a considerable effort; however, these efforts are not expected to call for major scientific innovation and discovery. Consequently, ecotoxicology has come to a transition phase and the field should assume a new role, which I believe is to assimilate with the part of ecology commonly denoted as "stress ecology". In this paper, I outline the transition and analyze the scientific basis of the new science.

Historically speaking

Before this transition is described, it is useful to look at the developments over the past three decades (see also "Three decades of ecotox texts" below). As ecotoxicology developed into a mature discipline in the 1980s and 1990s, profound changes also took place within ecology and the field became more diverse, for two reasons. First, molecular ecology appeared, which applied techniques from molecular biology to solve problems of population structure and adaptation (*22*); and second, systems ecology was introduced, which studies the behavior of complete ecosystems, including their interaction with the abiotic environment (*23*). Consequently, it became impossible for an ecologist to cover the complete spectrum, from molecules to systems, from the microlevel to the macrolevel.

The call for more "eco" in ecotoxicology did not specify what branch of ecology would be needed to illuminate ecotoxicology (*24–28*). Kareiva et al. argued that ecology itself had only recently begun to provide the necessary tools that could be useful for predicting toxic effects (*29*). These authors believed that stage–structure demographic modeling, community theory, and spatial analysis were three fields in which ecology and ecotoxicology could meet. Similarly, Løkke and I identified three areas in ecology of relevance to ecotoxicology, namely molecular population analysis, life-history theory (including reaction norms), and community analysis using food webs (*30*).

Thus, in the 1990s, many attempts were made to integrate ecological issues into ecotoxicology, but without removing the strength of the "testing approach" using single species, communities, or microcosms. The ecological arguments helped to strengthen the science but had little impact on regulation. For example, environmental standards for toxicants continue to be based on total, rather than bioavailable, concentrations; food-web analysis has never made its way into regulation, and life-cycle toxicity tests are rarely used for standards. Only a few "successes" arose from the drive for more ecology into ecotoxicology, such as the acceptance of multispecies tests (community, enclosure, field) as valid regulatory instruments and the use of functional endpoints (primary production, decomposition) in addition to survival, growth, and reproduction of single species.

How will this situation change in the future? First, the "testing" part of ecotoxicology will become less important, because, as argued by Slooff, regulatory authorities will need less traditional data (*31*). Second, it is my belief that the ecological part of ecotoxicology will evolve into the subdiscipline of stress ecology

Three decades of ecotox texts

The content of textbooks is a good indicator of how a science develops. A scientific discipline can be said to truly exist when university students learn from a common knowledge base. Such a base will promote understanding between practitioners of the discipline, remove confusion about terminology, and create a common awareness of the goals and the methodology.

Ramade published the first textbook on ecotoxicology, *Écotoxicologie*, in French in 1977, and the book was translated into English only 10 years later (*5*, *6*). This book still bears the traces of environmental toxicology and pays a lot of attention to human health effects. The ecological aspects of the book focused mainly on food-chain transfer and the biomass pyramid of ecological communities. One can see a similar preoccupation with biomass pyramids in a more recent textbook on environmental toxicology (*7*). Butler laid out a number of important features of the new science of ecotoxicology, but this book was not intended for students (*8*).

Moriarty's *Ecotoxicology. The Study of Pollutants in Ecosystems* was the second important textbook of ecotoxicology and played a key role for a decade or so (*9*). Moriarty balanced the ecological aspects better than Ramade and did not rely as heavily on issues of human health. He paid attention to questions such as species differences in sensitivity to pesticides, ecological determinants of residues, industrial melanism, and prediction methods. Because the fundamental ecology in the first half of the book was badly integrated with the environmental chemistry and toxicology in the later chapters, one could argue in retrospect that it was a textbook of ecology and toxicology rather than ecotoxicology.

In the 1980s, several edited volumes that were not textbooks made important contributions to reinforcing the scientific basis of the field, such as those by Sheehan et al. (*10*), Cairns (*11*, *12*), and Levin et al. (*13*). These books increasingly integrated ecological issues into ecotoxicology. The main avenues included community ecology, leading to the idea of community toxicity testing, pond studies, and experimental fields; and systems ecology, leading to the development of ecological indicators, which were later crystallized into the concept of "ecosystem health" (*14*).

Ecological modeling—as a means to integrate toxicological effects into an ecological framework—was another issue that arose in the 1980s with Levin et al.'s book. A coherent modeling framework for ecotoxicology, based on physiological principles, was developed by Kooijman (*15*).

By the beginning of the 1990s, the scientific basis for a true integration of ecology and ecotoxicology was laid out, and textbooks provided a more or less complete overview (*16–19*). Although the coverage of ecology in these books varied, in general, real ecological issues—such as population analysis using life-history information, recovery processes, resistance and adaptation, competition and predation, structure and function, and engineering species—got sufficient attention. Other edited volumes specifically addressed the integration of ecology and ecotoxicology (*20*). The most comprehensive textbook available to date, by Newman, first appeared in 1998 (*21*).

and become a true part of ecology. To illustrate this scenario, it is useful to have a closer look at the science of ecology.

The predictive power of ecology

What guidelines may be derived from ecology to support the analysis of toxic effects in ecosystems? What general laws can ecology offer for a solid assessment of pollution? Non-ecologists often reply that ecology lacks the predictive power of physics and chemistry. Consequently, ecotoxicology can hardly profit from ecology. The argument often invoked is that ecological systems are very "complex" and contain so many interacting parts that, like the weather, behavior of the system as a whole is extremely sensitive to initial conditions and subtle changes in driving factors and therefore is hardly predictable. Egler put it this way: "Nature is not only more complex than we think. It is more complex than we can think" (*32*).

The issue of predictive capacity of ecology and the existence of ecological "laws" have been the subject of some interesting debates in the recent ecological literature (*33–37*). Lawton started the discussion by asking whether ecology has any general laws at all (*33*). The answer to such a question critically depends on what is meant by the word "law". Given a dictionary definition of "widely observable tendency", Lawton concluded that ecology indeed has few laws, although there are numerous patterns and "rules of thumb". The reason is that many ecological phenomena are contingent on the organisms involved and on their environment. Likewise, ecological experiments and observations often have no wider validity than the time, place, and conditions under which they occurred. All too often, the outcome of an experiment is different from earlier experiments but is not in conflict with them because the conditions may have changed. This irreproducibility of ecological science, coupled with ecologists' typical dislike for standardization or simpler experimental setups, makes consistent progress very difficult.

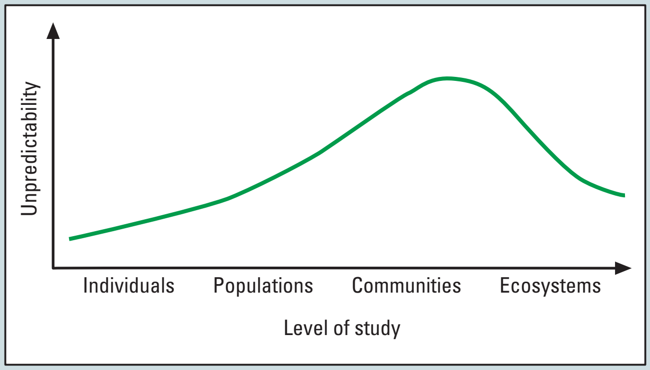
Unlike physicists, ecologists do not simplify their objects of study and analyze an idealized part of reality.

Yet, based on an extensive review of the literature, Lawton concluded that contingency and irreproducibility do not hold equally for all areas of ecology (*33*). In particular, he believes that repeatable patterns and rules are likely found at population-level (and below) and at the very large scales of complete ecosystems, while "the middle ground is a mess" (Figure 1). The underlying reason is that in simple systems (individuals and, to a certain extent, populations), contingencies are manageable and can be controlled by the experimenter; at the other end, in the realm of macroecology (systems ecology), the multitude of interactions average out and the general pattern emerges above the complexity. In the same spirit, Ghilarov expressed great doubt about the existence of ecological laws and argued that ecology is a collection of methodologies rather than a predictive science (*35*). Hengeveld and Walter took a similar view and argued that the only lawlike processes that operate in ecology derive from the constraints posed by physical and chemical laws (*38*).

FIGURE 1

Ecosystems are unpredictable

The qualitative graph demonstrates changes in unpredictability—defined as the absence of laws or the degree of contingency on initial conditions—in ecological systems as a function of hierarchical level of study (*32*).



Turchin, on the other hand, demonstrated that ecology does have lawlike propositions and can be considered a predictive science (*37*). When Turchin analyzed population ecology, he pointed out three long-standing foundational principles. First, according to the principle of exponential growth, as long as the environment experienced by the members of a population remains constant, all populations will change exponentially. Second, the principle of self-limitation says that for every population, the relative rate of increase decreases with density above some threshold. Third, on the basis of the principle of trophic oscillation, a pure consumer–resource system will inevitably exhibit unstable oscillations of density.

Turchin also argued that these principles can be considered true laws, comparable to the laws of physics, because they can be tested against observations and are not trivial (*37*). For example, if the principle of spontaneous generation were true, the first principle would not hold because populations would grow linearly, not exponentially. Weber holds a similar view and argued that the principle of competitive exclusion (where species cannot coexist if they use the same scarce resource) is a true ecological law because it is generally valid and testable, and it explains community structure (*39*).

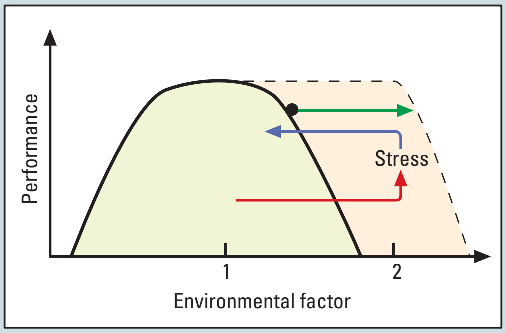
Another interesting observation is that "complexity" in ecology may derive directly from the question asked (*37*). Ecologists tend to ask very complicated questions; unlike physicists, they do not simplify their object of study and analyze an idealized part of reality. So, the rule that irreproducibility tends to decrease with increasing scale (see Figure 1) may also arise be-

cause macroecologists tend to ask simpler questions ("What is the rate of nitrification?") than community ecologists ("How many species should a community have?"). If the complexity is really in the question rather than the object, then this view has wide implications, refuting, for example, Egler's assertion that "ecosystems are more complex than we can imagine" (*32*).

FIGURE 2

Ecological niche and stress

The green-shaded area represents the ecological niche of a species. Stress arises when an environmental factor increases from point 1 to 2 such that the species is forced out of its ecological niche (red line). Various stress response reactions provide temporary survival under stress, and a return to the niche (blue line). If the borders of the niche are extended through adaptation, what was once stress is not stress any more (green line).



Determining the predictive power of ecology is very relevant for ecotoxicology. If the trend in Figure 1 is taken seriously, integration between ecology and ecotoxicology appears most profitable at the population level and below. Indeed, population ecotoxicology has become a well-developed field in which quantitative prediction, theory, and modeling have obtained a firm place (*40–48*).

Since its introduction into ecology, the appropriate definition of stress has been hotly debated.

Is stress ecology the future of ecotoxicology?

Toxic agents are clear examples of agents that stress biological systems. If ecotoxicologists are to find a place in ecology, they must be among those who study other stress factors, such as extremes in temperature, humidity, acidity, osmotic value, and nutrition. In fact, toxicants often interact with "natural" stress factors, especially when organisms are brought to the boundaries of their ecological amplitude—which is the range of environmental conditions over which an organism can survive and reproduce—and the effects of toxicants become more severe (*49*).

However, since its introduction into ecology, the appropriate definition of stress has been hotly debated (*50*). Ecologists now generally agree that a distinction should be made among a stressor (external factor), stress (an internal state brought about by a stressor), and stress response (a cascade of internal changes triggered by stress). Although the concept of stress can be defined at various levels of ecological integration (*51*), it is most commonly studied in the context of individual organisms (*52*), whereas stress responses are studied on the cellular and biochemical levels (*53*).

The concept of stress is not absolute and can only be defined with reference to the normal range of ecological function; that is, the ecological amplitude or ecological niche of the species. What is an extremely stressful condition for one organism, such as lack of air, is quite normal for another organism, such as fish. Incorporating this idea into a definition means that stress is a condition evoked in an organism by one or more environmental factors that bring the organism near or over the edges of its ecological niche. In addition, stress is usually transient, involves specific physiological responses, and is accompanied by the induction of mechanisms that counteract its consequences.

Figure 2 schematically illustrates this niche-based definition of stress. A situation of stress arises when some environmental factor changes and an organism finds itself outside its ecological niche. This will hold for that specific organism but maybe not for others. By definition, the organism cannot grow and reproduce outside its niche, but it may survive temporarily.

The stress can be relieved by moving back to the niche (by using behavioral mechanisms or suppressing the stressor) or changing the boundaries of the niche (by genetic adaptation). The first option must be accompanied by temporary physiological adaptation, which allows survival until the stressor is gone. The two options may be likened to the proverbial dilemma of Mohammed going to the mountain or the mountain moving. Calow made a similar observation when he distinguished between the proximate and ultimate responses to stress (*54*).

The concept of niche must be specified further, because it is often not a property of a whole species and may vary between populations of a single species. In the latter case, a species with a wide ecological amplitude (a euryoecious species) may consist of several local populations, each with a narrow amplitude (stenoecious populations). Consequently, what one population experiences as stress is considered normal by another.

Physiologists have pointed out that a suite of different physiological indicators (e.g., heartbeat, blood glucose, oxygen consumption) jointly provide a better measure of the physiological state of an organism than a single variable (*55*, *56*). Physiological state (also called physiotype) may therefore be considered a multivariate property of an individual. Consequently, stress can be defined in terms of a deviation from the state in a multidimensional space.

Figure 3 depicts the multidimensional concept of stress. Stress is considered here in terms of two state variables, but the idea is easily generalized to more dimensions. Because the state of an organism will fluctuate over time without obvious adverse consequences, a particular range of operation should be considered “normal”. Kersting defined the 95% confidence space of undisturbed states as the normal operating range (NOR) of the system (*57*, *58*). Stress occurs if the combination of state variables falls outside the NOR. This multidimensional concept of stress can also be applied at the level of communities or even ecosystems, in which the abundances of individual species can be considered as state variables. To quantify the rate of stress, Kersting introduced a quantity called normalized ecosystem strain, which is the relative distance between the state of a system and the border of the NOR (*57*, *58*). Long-term monitoring of *Daphnia* and *Chlorella* populations in a closed microcosm inspired this concept.

In addition, the concept of recovery is defined as the return to the NOR. On the individual level, strong homeostatic mechanisms and built-in “set points” often make it easy to establish when recovery has occurred. In communities or ecosystems, recovery is a more elusive concept. Domsch et al. have solved the problem by defining, for bacterial communities in soil, the range of inhibition by “natural stressors” from which recovery is always observed (*59*). Consequently, if a stressor has an inhibitory effect outside this range, recovery is not to be expected. Complications will arise if a system does not return to the NOR after a perturbation but continues to operate in another corner of the state space. This could imply that the system has more than one stable state, a situation that could lead to catastrophic shifts upon disturbance (*60*). In the case of toxicants, the NOR of a community may change due to pollution-induced community tolerance (PICT); stress is then relieved in a way analogous to genetic adaptation on the population level. In PICT, the average resistance of a community to a stress factor increases as sensitive species become less dominant or disappear (*61*).

Ecotoxicogenomics as the future

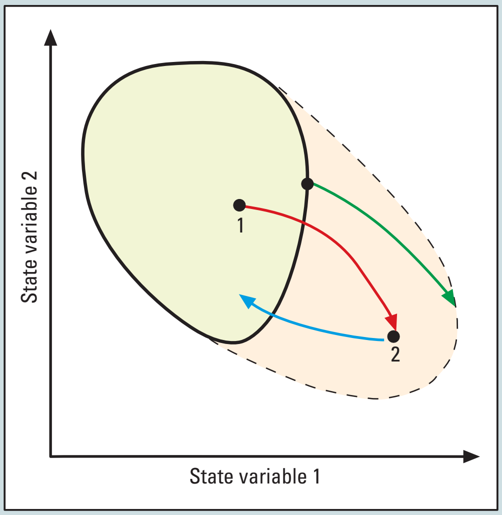
The application of multivariate statistics in ecotoxicology has been slowly growing since the 1980s. Reynoldson et al. used a multivariate (ordination) approach for describing the biological state of a benthic community (*62*). Landis et al. argued that multivariate statistics could be a basis for ecological risk assessment (*63*). Van den Brink and Ter Braak developed an approach (principal response curve analysis) that allows the effect of toxicants on a biological community to be expressed in terms of a single multivariate effect measure (*64*). Luoma et al. pointed out various strategies for separating environmental variability from stressor effects (*65*).

I have argued that new possibilities for the use of multivariate statistics in ecology lie ahead if ecotoxicologists follow the lines of bioinformatics (*66*). In a bioinformatics approach to ecological systems, the high degree of internal complexity is accepted as an inherent property, and consequently the state of the system must be analyzed in terms of possibly several thousand measurable variables. Using many defining variables greatly increases accuracy of the NOR (*66*). This possibility is now coming within experimental reach through the genomics revolution. In the near future, it is expected that microarrays that capture the “metagenome” of an ecosystem will become available (*67*). Such microarrays may contain, for example, DNA sequences from 5000 bacterial genes that are typical for a certain type of soil. By using the array, the expression pattern of a soil (up- and down-regulation of genes) may be established by competitive hybridization of complementary DNAs (*68*). Through repeated application on healthy soils, the NOR may be defined and stress may then be recognized as a deviation from the typical gene expression profile. Given the enormous number of targets analyzed simultaneously by a microarray, such an approach will allow an extreme degree of responsiveness and susceptibility.

FIGURE 3

Multivariate stress in a community

Stress may be defined graphically with multiple variables. This system example is characterized by two state variables, such as the abundances of two species in a community. All combinations of states in the absence of stress are designated as the normal operating range (NOR) (*51*). Once the NOR is defined (green region), stress is recognized by changing the state from 1 to 2 (red line), which is followed by a return to the NOR (blue line) or by expanding the NOR to encompass the new state (green line).



Thus, the merger between ecotoxicology and ecology may give rise to a new science at the crossroads of ecology, genomics, and bioinformatics. A new discipline called ecotoxicogenomics is expected to catalyze the transition of ecotoxicology into stress ecology (*69*).

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References

(1) Truhaut, R. *Ecotoxicol. Environ. Saf.* **1977**, *1*, 151–173.
(2) *Fundamentals of Aquatic Toxicology. Methods and Applications*; Rand, G. M., Petrocelli, S. R., Eds.; Hemisphere Publishing Corp.: Bristol, PA, 1985.
(3) *Handbook of Ecotoxicology*; Calow, P., Ed.; Blackwell Science: Cambridge, MA, 1993.
(4) *Handbook of Soil Invertebrate Toxicity Tests*; Løkke, H., Van Gestel, C. A. M., Eds.; Wiley & Sons: New York, 1998.
(5) Ramade, F. *Écotoxicologie*; Masson: Paris, France, 1977.
(6) Ramade, F. *Ecotoxicology*; Wiley & Sons: New York, 1987.
(7) Shaw, I. C.; Chadwick, J. *Principles of Environmental Toxicology*; Taylor & Francis: London, 1998.
(8) Butler, G. C. *Principles of Ecotoxicology*; Wiley & Sons: New York, 1978.
(9) Moriarty, F. *Ecotoxicology. The Study of Pollutants in Ecosystems*; Academic Press: New York, 1983.
(10) Sheehan, P. J.; Miller, D. R.; Butler, G. C.; Bourdeau, P. *Effects of Pollutants at the Ecosystem Level*; Wiley & Sons: New York, 1984.
(11) *Multispecies Toxicity Testing*; Cairns, J. J., Ed.; Pergamon Press: Elmsford, NY, 1985.
(12) *Community Toxicity Testing*; Cairns, J. J., Ed.; ASTM Special Publication Series. American Society for Testing and Materials: Philadelphia, PA, 1986.
(13) Levin, S. A.; Harwell, M. A.; Kelly, J. R.; Kimball, K. D. *Ecotoxicology: Problems and Approaches*; Springer-Verlag: New York, 1989.
(14) *Ecosystem Health*; Costanza, R., Norton, B. G., Haskell, B. D., Eds.; Island Press: Washington, DC, 1992.
(15) Kooijman, S. A. L. M. *Dynamic Energy Budgets in Biological Systems*; Cambridge University Press: New York, 1993.
(16) Van Straalen, N. M.; Verkleij, J. A. C. *Leerboek Oecotoxicologie*; VU-University Press: Amsterdam, The Netherlands, 1991.
(17) Forbes, V. E.; Forbes, T. L. *Ecotoxicology in Theory and Practice*; Chapman & Hall: New York, 1994.
(18) *Risk Assessment of Chemicals. An Introduction*; Van Leeuwen, C. J., Hermens, J. L. M., Eds.; Kluwer Academic Publishers: Norwell, MA, 1995.
(19) Walker, C. H.; Hopkin, S. P.; Sibly, R. M.; Peakall, D. B. *Principles of Ecotoxicology*; Taylor & Francis: London, 1996.
(20) *ECOtoxicology: Ecological Dimensions*; Baird, D. J., Maltby, L., Greig-Smith, P. W., Douben, P. E. T., Eds.; Chapman & Hall: New York, 1996.
(21) Newman, M. C. *Fundamentals of Ecotoxicology*; Lewis Publishers: Boca Raton, FL, 2001.
(22) *Genes in Ecology*; Berry, R. J., Crawford, T. J., Hewitt, G. M., Eds.; Blackwell Science: Cambridge, MA, 1992.
(23) Pahl-Wostl, C. *The Dynamic Nature of Ecosystems. Chaos and Order Entwined*; Wiley & Sons: New York, 1995.
(24) Koeman, J. H. *Ecotoxicol. Environ. Saf.* **1982**, *6*, 358–362.
(25) Cairns, J. J. *Regul. Toxicol. Pharmacol.* **1988**, *8*, 226–238.
(26) Maciorowski, A. F. *Environ. Toxicol. Chem.* **1988**, *7*, 677–678.
(27) Depledge, M. H. *Ambio* **1993**, *22*, 51–52.
(28) Calow, P. In *ECOtoxicology: Ecological Dimensions*; Baird, D. J., Maltby, L., Greig-Smith, P. W., Douben, P. E. T., Eds.; Chapman & Hall: New York, 1996; pp 5–12.
(29) Kareiva, P.; Stark, J.; Wennergren, U. In *ECOtoxicology: Ecological Dimensions*; Baird, D. J., Maltby, L., Greig-Smith, P. W., Douben, P. E. T., Eds.; Chapman & Hall: New York, 1996; pp 13–23.
(30) Van Straalen, N. M.; Løkke, H. In *Ecological Risk Assessment of Contaminants in Soil*; Van Straalen, N. M., Løkke, H., Eds.; Chapman & Hall: New York, 1997; pp 3–21.
(31) Slooff, W. *The Rise and Fall of Ecotoxicology*. In Essays on the Environment and Health Risks; Van Pol, R., Ed.; National Institute of Public Health and the Environment, Bilthoven, The Netherlands, Report 268826-003, 2003.
(32) Egler, F. E. *The Way of Science. A Philosophy of Ecology for the Layman*; Hafner Publishing Co.: New York, 1970.
(33) Lawton, J. H. *Oikos* **1999**, *84*, 177–192.
(34) Murray, B. G. J. *Oikos* **2000**, *89*, 403–408.
(35) Ghilarov, A. M. *Oikos* **2001**, *92*, 357–362.
(36) Ford, E. D.; Ishii, H. *Oikos* **2001**, *93*, 153–160.
(37) Turchin, P. *Oikos* **2001**, *94*, 17–26.
(38) Hengeveld, R.; Walter, G. H. *Acta Biotheor.* **1999**, *47*, 141–170.
(39) Weber, M. *Philosophy of Science* **1999**, *66*, 71–93.
(40) Marshall, J. S. *J. Fish. Res. Board Can.* **1978**, *35*, 461–469.
(41) Gentile, J. H.; Gentile, S. M.; Hairston, N. G. J.; Sullivan, B. K. *Hydrobiologia* **1982**, *93*, 179–187.
(42) Kooijman, S. A. L. M. In *Multispecies Toxicity Testing*; Cairns, J. J., Ed.; Pergamon Press: Elmsford, NY, 1985; pp 143–164.
(43) Sibly, R. M.; Calow, P. *Biol. J. Linn. Soc.* **1989**, *37*, 101–116.
(44) Van Straalen, N. M.; Kammenga, J. E. In *Ecotoxicology*; Schüürmann, G., Markert, B., Eds.; Wiley & Sons: New York; Spektrum Akademischer Verlag: Heidelberg, Germany, 1998; pp 621–644.
(45) Forbes, V. E.; Calow, P. *Environ. Toxicol. Chem.* **1999**, *18*, 1544–1556.
(46) Kammenga, J. E.; Van Koert, P. H. G.; Koeman, J. H.; Bakker, J. *Ecol. Appl.* **1997**, *7*, 726–734.
(47) *Demography in Ecotoxicology*; Kammenga, J. R., Laskowski, R., Eds.; Wiley & Sons: New York, 2000.
(48) Maltby, L.; et al. In *Ecological Variability: Separating Natural from Anthropogenic Causes of Ecosystem Impairment*; Baird, D. J., Burton, G. A., Eds.; Society of Environmental Toxicology and Chemistry: Boca Raton, FL, 2001, pp 27–82; ISBN 1-880611-43-0.
(49) Heugens, E. H. W.; Hendriks, A. J.; Dekker, T.; Van Straalen, N. M.; Admiraal, W. *Crit. Rev. Toxicol.* **2001**, *31*, 247–284.
(50) Grime, J. P. *Biol. J. Linn. Soc.* **1989**, *37*, 3–17.
(51) Parker, E. D., Jr.; et al. *Oikos* **1999**, *86*, 179–184.
(52) Maltby, L. *Ecological Applications* **1999**, *9*, 431–440.
(53) Korsloot, A. An Analysis of the Interdependence and Coordination of Cellular Stress Defense Systems in Arthropods, Ph.D. Thesis, Institute of Ecological Science, Amsterdam; Vrije Universiteit, Amsterdam, 2002.
(54) Calow, P. *Biol. J. Linn. Soc.* **1989**, *37*, 173–181.
(55) Depledge, M. H. *Ambio* **1989**, *18*, 301–302.
(56) Depledge, M. H. *Ambio* **1990**, *19*, 251–252.
(57) Kersting, K. *Ecol. Bull.* **1984**, *36*, 150–153.
(58) Kersting, K. *Verh. Int. Ver. Theor. Angew. Limnol.* **1987**, *23*, 1641–1646.
(59) Domsch, K. H.; Jagnow, G.; Anderson, T.-H. *Residue Rev.* **1983**, *86*, 65–105.
(60) Scheffer, M.; Carpenter, S.; Foley, J. A.; Folke, C.; Walker, B. *Nature* **2001**, *413*, 591–596.
(61) Boivin, M.-E.; Breure, A. M.; Posthuma, L.; Rutgers, M. *Human and Ecological Risk Assessment* **2002**, *8*, 1035–1055.
(62) Reynoldson, T. B.; Bailey, R. C.; Day, K. E.; Norris, R. H. *Australian Journal of Ecology* **1995**, *20*, 198–219.
(63) Landis, W. G.; Matthews, G. B.; Matthews, A. J.; Sergeant, A. *Environ. Toxicol. Chem.* **1994**, *13*, 1917–1927.
(64) Van den Brink, P. J.; Ter Braak, C. J. F. *Environ. Toxicol. Chem.* **1999**, *18*, 138–148.
(65) Luoma, S. N.; et al. In *Ecological Variability: Separating Natural from Anthropogenic Causes of Ecosystem Impairment*; Baird, D. J., Burton, G. A., Eds.; Society of Environmental Toxicology and Chemistry: Boca Raton, FL, 2001; pp 141–177.
(66) Van Straalen, N. M. *Biodegradation* **2002**, *13*, 41–52.
(67) Rondon, M. R.; et al. *Appl. Environ. Microbiol.* **2000**, *66*, 2541–2547.
(68) DeRisi, J. L.; Iyer, V. R.; Brown, P. O. *Science*, **1997**, *278*, 680–686.
(69) Neumann, N. F.; Galvez, F. *Biotechnol. Adv.* **2002**, *20*, 391–419.

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